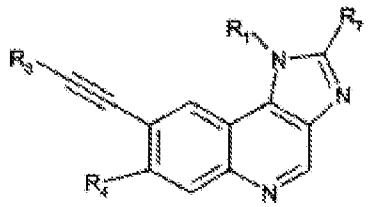
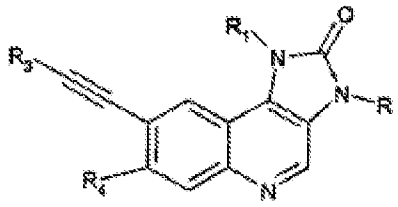
DETAILED ACTION

Applicants have elected group I of the restriction. Claims 1-5, 9-11 drawn to compounds of



(Ia)

formula Ia and Ib



(Ib)

wherein R7 is a H, R3 is a pyridyl or a phenyl and R1 is a phenyl.

Applicant's election of Group I in the reply filed on 4/12/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 2-5, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 9-11 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R3 to be a phenyl or a pyridyl substituted by a single substitutent such a

> and are independently selected from halo (e.g. Cl or F); cyano; cyano lower alkyl (e.g. cyanomethyl, cyanoethyl and cyanopropyl); lower alkyl; lower alkoxy; amino; amino-lower alkyl; amino-lower alkoxy; amino-lower alkyl sulfanyl or thiol-lower alkyl;

does not reasonably provide enablement for

> cyclopropyl); or R_8 and R_9 together with the N atom form a 3- to 8-membered heterocyclic ring containing 1-4 nitrogen, oxygen or sulfur atoms (e.g. azetidinyl, pyrrolidinyl, piperidino, morpholinyl, imidazolinyl, piperazinyl or lower alkyl-piperazinyl)]; amino-carbonyl-lower alkyl (e.g. R_8R_9-N-C(O)-CH_2-, wherein R_8 and R_9 are as defined above); heterocyclyl; heterocyclyl-lower alkyl; heterocyclyl-lower alkoxy or heterocyclyl-lower alkanesulfanyl wherein the heterocyclyl is a 3- to 8-membered heterocyclic ring containing 1-4 nitrogen, oxygen or sulfur atoms (e.g. imidazolyl, imidazolinyl, pyrrolidinyl, morpholinyl, azetidinyl, pyridyl, piperidino, piperidyl, piperazinyl or lower alkyl-piperazinyl); wherein alkyl may be linear or cyclic (e.g. cyclopropyl) and the alkyl in any of the substituents above may optionally be substituted with -NR_8R_9, wherein R_8 and R_9 are as defined above;

nor for the definition of R2-R6 to be any organic moiety. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is a (highly) substituted tricylic compound that is useful in pharmaceuticals.

3) The state of the prior art: Regarding how to use : The state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment of diseases as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Regarding how to make :-
It is not easy to synthesis compounds. It involves a the complicated interaction between the starting materials , reagents, reactants and other conditions such as temperature , pressure, catalyst , solvents and so on. Applicants claims generically state any "organic moiety " have numerous substitutents R4, R5, R6 , R to be huge large groups. Dorwald et al.
As stated in the preface to a recent treatise:

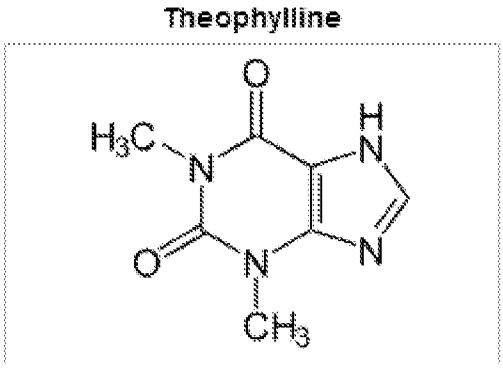
"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research

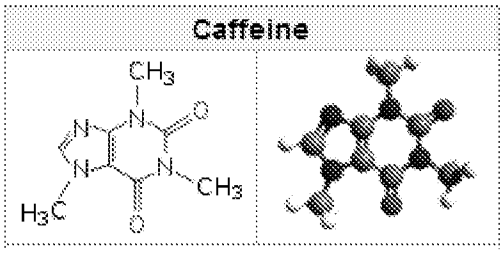
chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also

show different properties, for e.g. theophylline 

and caffeine. 

One of them is a bronchodilator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the R's having the various substituents,

7) The existence of working examples: The instant specification does not have any working examples. All the examples have small substituents . In the specification there is a vague description on page 34 such as

> wherein functional groups which are present in the starting compounds in processes a) to c) and are not intended to take part in the reaction, are present in protected form if necessary, and protecting groups that are present are cleaved, wherein said starting compounds may also exist in the form of salts provided that a salt-forming group is present and a reaction in salt form is possible.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, and the prior art compounds also do disclose close compounds which do not have all these various substituents., the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

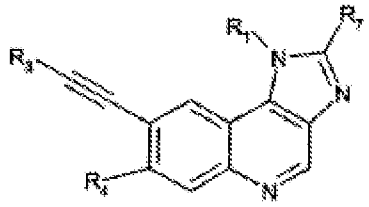
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

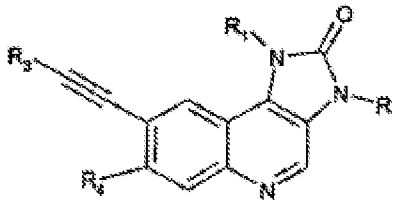
Claims 1-5, 9and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 2004 /058759 3M Innovatives Properties..

Applicants claims are drawn to compounds of the generic formula



(Ia)

and



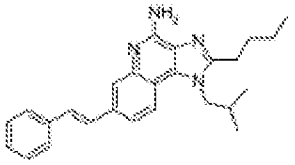
(Ib)

Scope & Content of Prior Art MPEP 2141.01

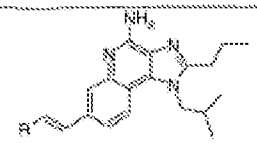
The WO document teaches compounds of the same core and similar compounds , see eg 7, 112, 122, 495, see pages 271, 313, 315 for example.

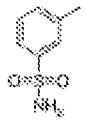
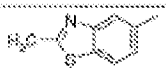
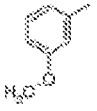
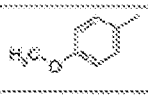
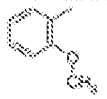
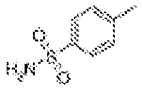
Example 7

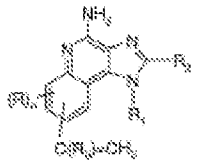
3-Butyl-1-isobutyl-7-[(*E*)-2-phenylethenyl]-1*H*-imidazo[4,5-*c*]quinolin-4-amine



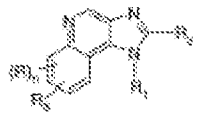
Examples 440-455



Example	Aryl- or Heteroaryl halide	R
440	3-Bromobenzenesulfonamide	
441	3-Bromo-2-methylbenzothiazole	
442	2-Iodo-5-methylthiophene	
443	3-Bromoanisole	
444	4-Bromoanisole	
445	2-Bromoanisole	
446	3-Bromopyridine	
447	4-Bromobenzenesulfonamide	



XLVII



XLVIII

On page 27 it discloses the 2 formulas and R3 is Z Ar and Z is a bond or an alkylene , alkenylene or an alkynylene

The reference teaches the equivalence of these groups.

Difference between Prior Art and the claims MPEP 2141.02

The difference is in the double bond v triple bond.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

The prior art teaches the equivalency of the single , double and triple bond on the compounds with the same core. This would motivate a person of skill in the art to make more compounds with the variations taught in the prior art. Besides the prior art discloses several compounds with the double bond too as given above, further motivating a person the make similar compounds with the triple bond.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 9-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-21 of copending Application No. 10/515126. Although the conflicting claims are not identical, they are not patentably distinct

from each other because the compounds are also drawn to the same core wherein one of the R substitutent is an alkenyl or an alkinyl and which are further substituted.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-5, 9-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1-5 of copending Application No. 10/579587. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same core and also have the same activity.

Absence any showing of unexpected results these are obvious variations especially in view of WO 2004 /058759.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Also rejected under ODP over claims 1-5 of US 12/792187 and 1-5 of US 12/792471. for the same reasons as given above.

Conclusion

Claims 1-5, 9-11 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

June 3, 2010.